MDA-MB-175 cells or from another source, such as another animal species, but also the polypeptide prepared by recombinant or synthetic methods. It also includes variant forms including functional derivatives, allelic variants, naturally occurring isoforms and analogues thereof. Sometimes the γ-HRG is "native γ-HRG" which refers to endogenous γ-HRG polypeptide which has been isolated from a mammal. The γ-HRG can also be "native sequence γ-HRG " insofar as it has the same amino acid sequence as a native γ-HRG (e.g. human γ-HRG shown in FIG. 7A-7C). Amino acid sequence variants of the native sequence are prepared by introducing appropriate nucleotide changes into the native sequence DNA, or by in vitro synthesis of the desired polypeptide. Such variants include, for example, deletions from, or insertions or substitutions of, residues within the amino acid sequence shown for the human protein in FIG. 7A-7C as generally described above for other heregulin. Any combination of deletion, insertion, and substitution is made to arrive at the final construct, provided that the final construct possesses the desired characteristics. The amino acid changes also may alter post-translational processes of the native sequence, such as changing the number or position of O-linked glycosylation sites.

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IN THE CLAIMS

Please cancel claim 13.

Please amend claims 1-7, 9, and 14-17 to read as follows:

1. (Amended) A method of inducing hair cell generation or inner-ear-supporting cell growth, regeneration, and/or proliferation, comprising contacting an inner-ear-supporting cell which expresses HER2 and/or HER3 receptors with an effective amount of an isolated ligand which activates HER2 and/or HER3 receptors, said isolated ligand comprising a heregulin polypeptide selected from the group consisting of heregulin-β2 (SEQ ID NO: 5), heregulin-β2-like polypeptide (SEQ ID NO: 9), heregulin-β3 (SEQ ID NO: 7), heregulin γ (SEQ ID NO: 11), heregulin-α (SEQ ID NO: 1) variants, heregulin-β1 (SEQ ID NO: 3) variants, heregulin-β2 (SEQ ID NO: 5) variants, heregulin-β2-like polypeptide (SEQ ID NO: 9) variants, heregulin-β3 (SEQ ID NO: 7) variants, heregulin γ (SEQ ID NO: 11) variants, heregulin-α (SEQ ID NO: 1) fragments, heregulin-β1 (SEQ ID NO: 3) fragments, heregulin-β2 (SEQ ID NO: 5) fragments, heregulin-β2-like polypeptide (SEQ ID NO: 9) fragments, heregulin-β3 (SEQ ID NO: 7)

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fragments, heregulin γ (SEQ ID NO: 11) fragments, heregulin agonist antibody and heregulin agonist antibody fragments.

2. (Amended) The method of claim 1, wherein the activating ligand is a heregulin-α variant, heregulin agonist antibody or fragment thereof capable of binding to the HER2 or HER3 receptor, wherein said heregulin-α variant is selected from the group of heregulin-α variants having an amino acid substitution, deletion or insertion at one or more amino acid residues corresponding to positions 2, 3, 8, 9, 23, 24, 33, 34, 36, 37, 42, 43, 45, 46, 48, 49, 62-67, 86, 87, 110, 111, 123, 124, 134, 135, 142, 143, 151, 152, 164-166, 170-172, 208-218, 226-254, 256-265, 272, 273, 278, 279, 285-309, 437, and 608- 611 in the heregulin-α amino acid sequence of SEQ ID NO: 1.

3. (Amended) The method of claim 1, wherein the activating ligand is a human heregulin polypeptide or a fragment thereof.

4. (Amended) The method of claim 1, wherein the activating ligand is selected from the group consisting of HRG-α variants, -β1 variants, -β2, -β2 variants, -β2-like polypeptide, -β2-like polypeptide variants, -β3, and -β3 variants, and fragments thereof.

5. (Amended) The method of claim 1, wherein the activating ligand is γ-HRG or a variant or a fragment thereof.

6. (Amended) The method of claim 1, wherein the activating ligand is a recombinant human heregulin polypeptide or a fragment thereof.

7. (Amended) The method of claim 1, wherein the supporting cell is in a cochlear implant.

9. (Amended) The method of claim 1, wherein the activating ligand is a heregulin agonist antibody.

14. (Amended) A method of increasing the number of inner-ear-supporting cells, comprising administering to a patient in need thereof an effective amount of an isolated HER2 and/or HER3 activating ligand comprising a heregulin polypeptide selected from the group consisting of heregulin-β2 (SEQ ID NO: 5), heregulin-β2-like polypeptide (SEQ ID NO: 9), heregulin-β3 (SEQ ID NO: 7), heregulin γ (SEQ ID NO: 11), heregulin-α (SEQ ID NO: 1) variants, heregulin-β1 (SEQ ID NO: 3) variants, heregulin-β2 (SEQ ID NO: 5) variants, heregulin-β2-like polypeptide (SEQ ID NO: 9) variants, heregulin-β3 (SEQ ID NO: 7) variants, heregulin γ (SEQ ID NO: 11) variants, heregulin-α (SEQ ID NO: 1) fragments, heregulin-β1 (SEQ ID NO: 3) fragments, heregulin-β2 (SEQ ID NO: 5) fragments, heregulin-β2-like polypeptide (SEQ ID NO: 9) fragments, heregulin-β3 (SEQ ID NO: 7) fragments, heregulin γ (SEQ ID NO: 11) fragments, heregulin agonist antibody and heregulin agonist antibody fragments.

15. (Amended) The method of claim 14, wherein the activating ligand is a heregulin-α variant, heregulin agonist antibody or fragment thereof capable of binding to the HER2 or HER3 receptor, wherein said heregulin-α variant is selected from the group of heregulin-α variants having an amino acid substitution, deletion or insertion at one or more amino acid residues corresponding to positions 2, 3, 8, 9, 23, 24, 33, 34, 36, 37, 42, 43, 45, 46, 48, 49, 62-67, 86, 87, 110, 111, 123, 124, 134, 135, 142, 143, 151, 152, 164-166, 170-172, 208-218, 226-254, 256-265, 272, 273, 278, 279, 285-309, 437, and 608- 611 in the heregulin-α amino acid sequence of SEQ ID NO: 1.

16. (Amended) A method of treating a hair cell related hearing disorder, comprising administering to a patient in need thereof an effective amount of an isolated HER2 and/or HER3 activating ligand comprising a heregulin polypeptide selected from the group consisting of heregulin-β2 (SEQ ID NO: 5), heregulin-β2-like polypeptide (SEQ ID NO: 9), heregulin-β3 (SEQ ID NO: 7), heregulin γ (SEQ ID NO: 11), heregulin-α (SEQ ID NO: 1) variants, heregulin-β1 (SEQ ID NO: 3) variants, heregulin-β2 (SEQ ID NO: 5) variants, heregulin-β2-like polypeptide (SEQ ID NO: 9) variants, heregulin-β3 (SEQ ID NO: 7) variants, heregulin γ (SEQ ID NO: 11) variants, heregulin-α (SEQ ID NO: 1) fragments, heregulin-β1 (SEQ ID NO: 3) fragments, heregulin-β2 (SEQ ID NO: 5) fragments, heregulin-β2-like

polypeptide (SEQ ID NO: 9) fragments, heregulin-β3 (SEQ ID NO: 7) fragments, heregulin γ (SEQ ID NO: 11) fragments, heregulin agonist antibody and heregulin agonist antibody fragments.

17. (Amended) The method of claim 16, wherein the activating ligand is a heregulin-α variant, heregulin agonist antibody or fragment thereof capable of binding to the HER2 or HER3 receptor, wherein said heregulin-α variant is selected from the group of heregulin-α variants having an amino acid substitution, deletion or insertion at one or more amino acid residues corresponding to positions 2, 3, 8, 9, 23, 24, 33, 34, 36, 37, 42, 43, 45, 46, 48, 49, 62-67, 86, 87, 110, 111, 123, 124, 134, 135, 142, 143, 151, 152, 164-166, 170-172, 208-218, 226-254, 256-265, 272, 273, 278, 279, 285-309, 437, and 608- 611 in the heregulin-α amino acid sequence of SEQ ID NO: 1.

Please add the following new claims:

19. (New) The method of claim 1, wherein the activating ligand is a heregulin-β variant, heregulin agonist antibody, or fragment thereof capable of binding to the HER2 or HER3 receptor, wherein said heregulin-β variant is selected from the group consisting of heregulin-β variants having an amino acid substitution at one or more amino acid residues corresponding to positions S177, H178, L179, V180, K181, E184, E186, K187, T188, V191, N192, G193, G194, E195, M198, V199, K200, D201, N204, P205, S206, R207, Y208, L209, K211, P213, N214, E215, T217, G218, D219, Q222, N223, Y224, M226, S228, and F229 of SEQ ID NO: 5, SEQ ID NO: 7, or SEQ ID NO: 9, or of the mature polypeptide within SEQ ID NO: 3.

20. (New) The method of claim 14, wherein the activating ligand is a heregulin-β variant, heregulin agonist antibody, or fragment thereof capable of binding to the HER2 or HER3 receptor, wherein said heregulin-β variant is selected from the group consisting of heregulin-β variants having an amino acid substitution at one or more amino acid residues corresponding to positions S177, H178, L179, V180, K181, E184, E186, K187, T188, V191, N192, G193, G194, E195, M198, V199, K200, D201, N204, P205, S206, R207, Y208, L209, K211, P213, N214, E215, T217, G218, D219, Q222, N223, Y224, M226, S228, and F229 of SEQ ID NO: 5, SEQ ID NO: 7, or SEQ ID NO: 9, or of the mature polypeptide within SEQ ID NO: 3.